Purpose : This document brings together the most common questions neurosurgeons ask during calls and visits—along with clear, ready-to-use answers. It's designed as a handy guide to help our Sales and Customer Success teams feel confident and well-prepared in every conversation.

Questions around the workflow:

1. **How much time does your MRI protocol add?**
   Our routine protocol includes 3D structural imaging (T1, FLAIR, T2, and post-contrast), along with additional rs-fMRI and DTI sequences. The advanced sequences typically take 10–15 minutes, depending on the scanner and field strength. Since we use 3D structural sequences, if your inherent brain protocol already includes 3D (T1, FLAIR, T2, and post-contrast), then only 10–15 minutes are added. If it is 2D, we will need to replace them with 3D, which may alter scan time accordingly.

2. **Will I be able to use the same protocol for my neuronavigation or do I need to acquire additional MRIs?**
   The imaging protocol we establish is versatile and can also be utilized for neuronavigation, eliminating the need for additional imaging specifically for that purpose. We recommend acquiring images using our standardized structural imaging protocols as they help us maintain consistency and reproducibility.

3. **Does this work both on sedated and non-sedated patients? Will the network maps from rfMRI be different for sedation vs non sedation?**
   Yes, our protocol works for both sedated and non-sedated patients. However, it is important to note that rs-fMRI-derived network maps are influenced by sedation, varying based on the type of sedative, its dosage, and the depth of sedation. Typically, higher-order networks such as the Default Mode Network (DMN), Dorsal Attention Network (DAN), Salience Network, and Central Executive Network (CEN) show reduced connectivity under sedation. In contrast, lower-order sensory networks, including the Sensorimotor Network (SMN), Visual Network (VN), and Auditory Network (AN), may maintain or even exhibit increased activity.
   For accurate and reliable results, we recommend avoiding sedation unless it is absolutely necessary.

4. **What is the current workflow for sharing scans with BrainSightAI and receiving processed results?**
   Scans can be uploaded directly to our secure cloud platform VoxelBox Explore or transferred via PACS. Once received, they are processed on our platform and made available for download within **15 hours** of upload. This timeline also includes the internal QA/QC review by our in-house radiologist to ensure that we share the most accurate results with you. The processed outputs are fully compatible with leading **neuronavigation systems and other dicom viewers**, making it seamless to integrate into clinical workflows.

Follow up questions we can ask the clinicians -

1. What is your current average MRI scan time for brain tumor patients?
2. Do you use any neuronavigation system currently? If yes - which one?
3. Are there any particular imaging format requirements or export settings you'd need us to be compatible with?
4. How often do you need to sedate patients for MRI — and what sedation protocols do you typically follow?

Question around the technology and use cases:

5. **Can you provide me with the list of networks and tractography that BrainSightAI provides?**
   List of networks -

1. Sensorimotor area
2. Auditory area
3. Default Mode network
4. Dorsal Attention network
5. Salience network
6. Central executive network
7. Ventral attention network
8. Visual area
9. Ventral premotor cortex
10. Language
    a. Language primary
        i. Language primary (combined mask)
        ii. Broca's area
        iii. Wernicke's area
        iv. Inferior frontal motor speech area
        v. Inferior parietal sensory speech area
        vi. Posterior temporal sensory speech
        vii. Superior temporal sensory speech
    b. Language secondary combined
    c. Language tertiary combined

List of tracts -

- Corticospinal Tract (CST)
- Arcuate Fasciculus (AF)
- Frontal Aslant Tract (FAT)
- Superior Longitudinal Fasciculus (SLF) - Divided into SLF 1,2 & 3
- Inferior Longitudinal Fasciculus (ILF)
- Inferior Fronto-Occipital Fasciculus (IFOF)
- Corpus Callosum
- Optic Radiation (OR)

5. I understand your commercial product or approved product is for 12 networks but do you have a research or experimental product that can provide me with more networks?

We are eager to collaborate with physicians across diverse specialties to better understand their unique clinical needs for various disorders. Our goal is to integrate additional networks thoughtfully, while carefully balancing technical feasibility and time constraints.

6. I do a lot of work with epilepsy? Can you provide me with more networks for epilepsy?

Most of the networks we currently provide are relevant to epilepsy as they are often affected by the condition. For specific indications like epilepsy, we can offer additional networks such as the medial temporal network, which is crucial for memory. However, we are still in the process of developing networks relevant to epilepsy. We would be delighted to collaborate with you to further enhance our offerings for epilepsy and better address clinical needs in this area.

7. How do you ensure that motion or other factors do not affect the results?
rsfMRI and DTI are sensitive to motion, and significant distortions or motion artifacts can impact the quality of the results. If motion exceeds a certain threshold, it can compromise the accuracy of the sequences, rendering them unsuitable for processing. Therefore, minimizing patient motion during scanning is essential to ensure reliable and interpretable data. We have pre-set thresholds to accommodate for patient motion and a robust motion correction algorithm.

8. Why do I see activations in areas where I am not expecting?
This is a common and important question, especially in cases involving **brain tumors**. There are both technical and biological reasons that may contribute to unexpected or seemingly erroneous activations in fMRI results.

1. Biological Factors (Tumor-related)

- Disruption of Neurovascular Coupling: fMRI relies on the principle that increased neural activity leads to increased blood flow (neurovascular coupling). However, in tumor-affected regions—especially intra- and peri-tumoral areas—this coupling is often disrupted. This can lead to false negatives (missed activations) or false positives (spurious activations).

- Angiogenesis & Metabolic Noise: Tumors, particularly high-grade and aggressive ones, can create abnormal blood vessel growth to meet their oxygen demand. This can result in increased blood flow and oxygenation levels inside the tumor that mimic real BOLD signals, even in the absence of neural activity.

- True Activations in Tumor Regions: Studies (e.g., PubMed ID: 35023218) show that in diffuse, infiltrative tumors, portions of the tumor mass can still exhibit functional connectivity with healthy regions. Approximately 33% of tumor volume may remain functionally active in such cases—especially in low-grade gliomas.

2. Technical Factors

- Motion & Physiological Noise: Despite preprocessing steps, subject motion and physiological artifacts (heartbeat, breathing, etc.) can still cause spurious signals that appear as activations.

- Template Misalignment & Coregistration Issues: Large tumors can distort brain anatomy, making coregistration and segmentation difficult. This may result in slight misalignments between functional and structural images, or template mismatches, causing activations to appear inaccurately located.

- Partial Volume Effects & Smoothing: Spatial smoothing during fMRI processing can cause signal "spill-over" from adjacent active regions—particularly near tumor boundaries—resulting in activations appearing within or near the tumor.

- Denoising Limitations: Tumors can have intensity characteristics similar to some brain tissues, making it challenging to differentiate signal from noise during preprocessing.

3. Interpreting Uncertain Activations

- When activations appear in or around tumor regions, they may be true, false, or ambiguous. Their interpretation should always consider:
    - The grade and nature of the tumor
    - Structural imaging (T1, T2, FLAIR, T1+C)
    - Clinical experience and surgical planning context
    - If in eloquent areas, Direct Cortical Stimulation (DCS) can help confirm true functionality

- Histopathological confirmation post-surgery is the only way to determine definitively whether neural tissue was present in regions showing activation. Therefore, caution is advised, and interpretation must be nuanced.

10. What are the clinical validation studies that you have today?
Validation studies, 10 internal study reports, 5 + clinical ongoing studies
rsfMRI based Network against DCS - >35 subjects across different hospital centers for language and sensorimotor
rsfMRI based network against task based fMRI -
N= 75 healthy subjects
> 98 % specificity
Task is a subset of resting
Patient studies - analysis in progress

Validation of probabilistic tractography and diffusion metrics -

External feedback on tractography collected from intended users (neurosurgeons, neuroradiologists, and radiologists) incrementally on more than 1500 post-processed results. Systematically through clinical studies (N=34)
Internal Validation of scalar metrics in healthy subjects (N=10), tumor (N=15) & dementia cases (N=17)

Validation of algorithms - Our processing & inference algo have been tested and validated through a number of methods that include literature review, Qualitative and quantitative evaluation on healthy and clinical datasets including edge cases against a carefully defined acceptance criteria

There is one prospective clinical validation study done by a clinician on language in a case series - Dr. Abhiram Chandra Gabbita
https://actascientific.com/ASNE/pdf/ASNE-08-0852.pdf

11. Why is the area for language diffused? I do not see this in the task based fMRI

In resting-state fMRI (rs-fMRI), the area for language often appears more diffused compared to task-based fMRI because rs-fMRI reflects the intrinsic connectivity of brain networks during a resting state rather than activation tied to specific tasks. This diffusion represents the broader network of regions involved in language processing, including areas that are functionally connected but may not be directly activated in a task-based setting.

In task-based fMRI, activation is typically localized to specific regions corresponding to the given task (e.g., Broca's and Wernicke's areas for a language task like object naming or verb generation), resulting in a more focused map. What further contributes to the focus is the neuroradiologist thresholding the maps to remove all the sub par activations not directly related to the task like those in visual regions, or those due to noise. These result in localisation of primary language areas such as Broca’s and Wernicke’s. Resting-state fMRI, on the other hand includes areas that would typically be activated in a larger range of language tasks related like story comprehension, listening, reading, and semantic processing. Therefore, the regions go beyond typical Broca’s and Wernicke’s to also capture Inferior parietal sensory speech area, the precentral motor speech area, the supplementary speech area, frontal opercular, anterior insular, and several others, which some clinicians may not consider eloquent typically.

12. How does rsfMRI compare to tbFMRI? Why do I need rsMRI when I already do tbfMRI?

References -
https://pmc.ncbi.nlm.nih.gov/articles/PMC6051935/?utm_source=chatgpt.com

Resting-state fMRI (rsfMRI) offers several advantages over task-based fMRI (tbFMRI):

1. **No Task Requirement**: rsfMRI does not require active task performance, making it particularly suitable for children, cognitively impaired patients, or individuals with language barriers, where task compliance can be challenging.

2. **Comprehensive Network Mapping**: Unlike tbFMRI, which targets specific functions through predefined paradigms, rsfMRI simultaneously maps multiple brain networks, providing a broader picture of brain functionality.

3. **Time Efficiency**: rsfMRI requires only 8–10 minutes to map all networks, while tbFMRI can take 30–60 minutes depending on the number of paradigms tested, making rsfMRI more efficient for clinical workflows.

4. **Accuracy for Cognitive Networks**: Cognitive networks are mapped with higher accuracy using rsfMRI compared to tbFMRI, as rsfMRI captures intrinsic connectivity patterns that may not always be elicited by task performance.

Even if you currently use tbFMRI, rsfMRI complements it by offering a faster, more comprehensive, and patient-friendly solution, especially in cases where task performance is impractical or unreliable. It enhances diagnostic accuracy and expands the range of clinical applications.

Feature	rsfMRI	tbfMRI
Patient Demands	No task requirement — suitable for children, impaired, or sedated patients (pmc.ncbi.nlm.nih.gov)	Requires active compliance and specific tasks
Network Coverage	Maps multiple networks in one short acquisition	Targets one function per paradigm (language, motor, etc.)
Time Efficiency	8–10 minutes per full mapping	30–60 minutes depending on tasks
Accuracy & Specificity	Comparable accuracy for sensorimotor; greater specificity for language	Strong task activation but less lateralized
Clinical Feasibility	Reliable even when tbfMRI isn't possible	Standard in compliant patients

13. I would like to use this for DBS patients pre and post monitoring to see if surgery caused any problems. Is that something you have tried before?
We have not tried our algorithms in DBS surgeries. We would be happy to look into it, and collaborate with physicians to better understand what is needed.

14. Why are there activations in the tumor?

Activations within a tumor on fMRI may arise due to a mix of biological and technical factors. In infiltrative or low-grade gliomas, parts of the tumor may still contain functionally active neural tissue, resulting in true BOLD signals. However, tumors also alter normal blood flow through angiogenesis, leading to abnormally high oxygenation levels that can mimic neural activity—producing false positives. Additionally, neurovascular coupling, which drives BOLD signals, is often disrupted within and around tumors, complicating interpretation. Therefore, activations seen within tumor regions may represent either real functional tissue or vascular/metabolic noise, and should be interpreted alongside structural imaging and clinical judgment.
White paper - https://docs.google.com/document/d/1fKOvEN8axZtlW6fxH-Yd_qqgsipuUBvRsnWCPi3W1Tk/edit?tab=t.0

15. I want to understand how this works in brains that have suffered strokes at an early age and neuroplasticity has changed something?

Neuroplasticity allows the brain to reorganize neural pathways, enabling surviving neurons to form new connections and take over the functions of lost neurons. This process is particularly pronounced in early-life stroke, as the brain's heightened malleability during childhood often leads to more effective functional recovery over time.

Task-based fMRI (tb-fMRI) studies have shown that post-stroke recovery frequently manifests as increased activity in regions such as the ipsilesional sensorimotor and premotor cortex, the contralesional cerebellum, and the supplementary motor cortex. Resting-state fMRI (rs-fMRI) further reveals changes in connectivity, highlighting the reorganization of neural networks. For instance, children who experience dominant hemisphere often exhibit significant shifts in the lateralization of both structural and functional connectivity, with language functions transferring to the non dominant hemisphere. This phenomenon, captured by structural MRI and rs-fMRI studies, shows the non dominant hemisphere. developing greater lateralization compared to healthy controls.

While the use of fMRI in stroke has predominantly been limited to research, piloting rs-fMRI in clinical cases offers an opportunity to assess how neuroplasticity is reflected in resting-state derived networks. Theoretically, rs-fMRI should effectively capture these dynamic changes, providing valuable insights into recovery and network reorganization in the brain.

16. I do a lot of paediatric cases and would like to know if you are approved for paediatric use.

Our solution is not formally approved for pediatric use yet. Pediatric brains differ significantly from adult brains in size, morphology, myelination, signal profiles, and developmental trajectories. Using adult templates can introduce bias, and current pediatric templates are still limited, as there is no clear definition of "normal." Preliminary work—including AI-driven adaptive pipelines for pediatric brain mapping—is underway, but it requires further validation before clinical approval.

Reference:

https://www.google.com/url?q=https://docs.google.com/presentation/d/1jSiWGoo-7v2Km2zczZmH_GewMYF87C35qD_8jlfxtXc/edit?slide%3Did.g355fe19b3f1_0_111%23slide%3Did.g355fe19b3f1_0_111&sa=D&source=docs&ust=1755506167611539&usg=AOvVaw0D0U7a28WfofO8Zf4hqoKj

Follow up: When can we do pediatric cases on the BrainSightAI platform? -> Maybe early next year

17. How do you compare to Omniscient?

- Language Networks
    - *BrainSightAI* provides a nuanced breakdown of language networks into primary, secondary, and tertiary components, along with advanced hemispheric skew metrics (our terminology for lateralization). In upcoming releases, we'll further specify lateralization at Broca's, Wernicke's, and across all three language tiers.
- Cognitive Networks - Both platforms map core cognitive networks. We currently cover default-mode, executive, attention, sensorimotor, visual, and auditory domains, with enhanced segregation for language.
- BrainSightAI uses probabilistic tractography, which is more sensitive than the deterministic methods commonly used in other platforms. Soon, users will have the option to view both deterministic and probabilistic tract maps so they can choose based on clinical needs.

- Quicktome also offers advanced tractography integrated into neuronavigation tools.

Feature	**BrainSightAI**	**Quicktome (Omniscient)**
Language Networks	Primary/secondary/tertiary + lateralization depth	Holistic network maps
Cognitive Networks	Comprehensive mapping	Broad cognitive networks
Tractography	Probabilistic + option for deterministic	Advanced deterministic tracts
TMS Pre/Post Comparison	Included	Not emphasized
Custom Network Development	Coming soon—e.g., epileptogenic	Fixed connectome modules
Clinical Focus	Modular clinical application	Pre-surgical planning focus (pmc.ncbi.nlm.nih.gov, o8t.com, sciencedirect.com, hackensackmeridianhealth.org)

18. What are the different MRIs that your centre needs to have?

For BrainSightAI's advanced neuroimaging workflows, centres should have access to a clinical MRI scanner (1.5T or 3T preferred) equipped to run standard structural and advanced functional sequences. Specifically, the centre should be able to perform:

- **High-resolution 3D structural imaging** (T1, T2, FLAIR, and post-contrast)
- **Diffusion Tensor Imaging (DTI)** for mapping white matter pathways
- **Resting-state fMRI (rs-fMRI)** for functional network analysis

While these are the core requirements, most modern MRI scanners already support these sequences. A 3T scanner is ideal for higher signal-to-noise ratio and better spatial resolution, but BrainSightAI workflows can be adapted for 1.5T systems as well.

Follow up questions for the clinicians to

1. Do you currently use resting-state fMRI under sedation? If yes, how do you interpret those scans clinically?
2. Would it be helpful if we shared sample comparisons of rsfMRI under sedation vs. non-sedation?
3. What challenges do you face while interpreting functional data in infiltrative tumors?
4. Would you be open to a feedback loop with us to validate interpretations and help improve our algorithm?